SEQUENCE LISTING .

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<110> Ludmerer, Steven W.
      Graham, Donald J.
      LaFemina, Robert L.
      Flores, Osvaldo A.
      Pizzuti, Maura
      Traboni, Cinzia
<120> HCV REPLICONS CONTAINING NS5B FROM
  GENOTYPE 2B
<130> 21564YP
<140> 10/577,893
<141> 2006-05-01
<150> PCT/US2004/036575
<151> 2004-11-03
<150> 60/517,605
<151> 2003-11-05
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<222> (5)...(5)
<223> Xaa = threonine or serine
<221> VARIANT
<222> (24)...(24)
<223> Xaa = asparagine or serine
<221> VARIANT
<222> (31)...(31)
<223> Xaa = methionine or isoleucine
<221> VARIANT
<222> (392)...(392)
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Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile Glu
                        455
Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro His
                    470
                                         475
Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro Pro
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                                     490
Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu Ile
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            500
Ala Gln Gly Ala Arg Ala Ala Ile Cys Gly Arg Tyr Leu Phe Asn Trp
                             520
                                                  525
        515
Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser Arg
                        535
                                             540
Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Gly Asp Ile
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                                         555
Tyr His Ser Val Ser His Ala Arg Pro Arg Leu Leu Leu Cys Leu
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                565
                                     570
Leu Leu Ser Val Gly Val Gly Ile Phe Leu Leu Pro Asp Arg
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<211> 1776
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<223> n = A or T
<221> variation
<222> (9)...(9)
<223> n = C or A
<221> variation
<222> (13)...(13)
<223> n = A \text{ or } T
<221> variation .
<222> (15)...(15)
<223> n = A or C
<221> variation
<222> (21)...(21)
\langle 223 \rangle n - A or G
<221> variation
<222> (24)...(24)
<223> n = C or G
<221> variation
<222> (28)...(28)
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<223> n = T or C

<221> modified base

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<223> n = G \text{ or } C
<221> variation
<222> (33)...(33)
<223> n = C or A
<221> variation
<222> (71)...(71)
<223> n = A or G
<221> variation
<222> (83)...(83)
<223> n = G \text{ or } T
<221> variation
<222> (1174)...(1174)
<223> n = A or C
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acctcgagga gtgcctctct gagggcaaag aaggtgactt ttgacagggt gcaggtgctg 180
gacgcacact atgactcagt cttgcaggac gttaagcggg ccgcctctaa ggttagtgcg 240
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gtcgatttcc tcctcaaagc ttggggaagt aagaaggacc caatggggtt ctcgtatgac 660
accogctgct ttgactcaac cgtcacggag agggacataa gaacagaaga atccatatat 720
caggettgtt etetgeetca agaageeaga aetgteatae aetegeteae tgagagaett 780
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gcagcgtgta aggctgcagg gatcgtggac cctgttatgt tggtgtgtgg agacgacctg 960
gtcgtcatct cagagagcca aggtaacgag gaggacgagc gaaacctgag agctttcacg 1020
gaggctatga ccaggtattc cgccctccc ggtgaccttc ccagaccgga atatgacttg 1080
gagettataa cateetgete etcaaaegta teggtagege tggaeteteg gggtegeege 1140
eggtactice taaccagaga ecetaceact ceanteacee gagetgettg ggaaacagta 1200
agacactece etgteaatte ttggetggge aacateatee agtacgeece cacaatetgg 1260
gtccggatgg tcataatgac tcacttcttc tccatactat tggcccagga cactctgaac 1320
caaaatctca attttgagat gtacggggca gtatactcgg tcaatccatt agacctaccg 1380
gccataattg aaaggctaca tgggcttgaa gccttttcac tgcacacata ctctccccac 1440
gaacteteae gggtggeage aacteteaga aaacttggag egeeteeet tagagegtgg 1500
aagagteggg egegtgeegt gagagettea eteategeee aaggagegag ggeggeeatt 1560
tgtggccgct acctcttcaa ctgggcggtg aaaacaaagc tcaaactcac tccattgccc 1620
gaggcgagcc gcctggattt atccgggtgg ttcaccgtgg gcgccggcgg gggcgacatt 1680
tatcacageg tgtegeatge eegaceege ctattactee tttgeetact cetacttage 1740
gtaggagtag gcatcttttt actccccgat cqatqa
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<210> 3
<211> 1394
<212> PRT
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<223> modified NS3-5A
<221> VARIANT
<222> (1215)...(1215)
<223> Xaa = asparagine or serine
<221> VARIANT
<222> (904)...(904)
<223> Xaa = valine or alanine
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Cys Ile Ile Thr Ser Leu Thr Gly Arg Asp Lys Asn Gln Val Glu Gly
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Glu Val Gln Val Val Ser Thr Ala Thr Gln Ser Phe Leu Ala Thr Cys
Val Asn Gly Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr
                        55
Leu Ala Gly Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp
                    70
                                        75
Gln Asp Leu Val Gly Trp Gln Ala Pro Pro Gly Ala Arg Ser Leu Thr
                85
                                    90
Pro Cys Thr Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala
           100
                                105
                                                    110
Asp Val Ile Pro Val Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu
                                                125
                            120
Ser Pro Arg Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu
                        135
                                            140
Leu Cys Pro Ser Gly His Ala Val Gly Ile Phe Arg Ala Ala Val Cys
                   150
                                        155
Thr Arg Gly Val Ala Lys Ala Val Asp Phe Val Pro Val Glu Ser Met
               165
                                    170
Glu Thr Thr Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro
           180
                               185
Ala Val Pro Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly
                            200
                                                205
Ser Gly Lys Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr
                       215
Lys Val Leu Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly
                   230
                                        235
Ala Tyr Met Ser Lys Ala His Gly Ile Asp Pro Asn Ile Arg Thr Gly
                245
                                   250
Val Arg Thr Ile Thr Thr Gly Ala Pro Val Thr Tyr Ser Thr Tyr Gly
                                265
Lys Phe Leu Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile
                            280
                                                285
Ile Cys Asp Glu Cys His Ser Thr Asp Ser Thr Thr Ile Leu Gly Ile
                       295
                                           300
Gly Thr Val Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val
                    310
                                        315
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Leu Ala Thr Ala Thr Pro Pro Gly Ser Val Thr Val Pro His Pro Asn
                325
                                    330
Ile Glu Glu Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly
            340
                                345
Lys Ala Ile Pro Ile Glu Ala Ile Arg Gly Gly Arg His Leu Ile Phe
                            360
Cys His Ser Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Ser Gly
                        375
                                            380
Leu Gly Ile Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val
                    390
                                        395
Ile Pro Thr Ile Gly Asp Val Val Val Ala Thr Asp Ala Leu Met
                405
                                    410
Thr Gly Tyr Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys
            420
                                425
Val Thr Gln Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu
                            440
Thr Thr Thr Val Pro Gln Asp Ala Val Ser Arg Ser Gln Arg Arg Gly
                        455
Arg Thr Gly Arg Gly Arg Met Gly Ile Tyr Arg Phe Val Thr Pro Gly
                    470
                                        475
Glu Arg Pro Ser Gly Met Phe Asp Ser Ser Val Leu Cys Glu Cys Tyr
                                    490
                                                        495
Asp Ala Gly Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Ser Val
                                505
Arg Leu Arg Ala Tyr Leu Asn Thr Pro Gly Leu Pro Val Cys Gln Asp
                            520
                                                525
His Leu Glu Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp
                        535
                                            540
Ala His Phe Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr
                    550
                                        555
Leu Val Ala Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro
                565
                                    570
Pro Ser Trp Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr
           580
                                585
                                                    590
Leu His Gly Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn
                           600
                                                605
Glu Val Thr Leu Thr His Pro Ile Thr Lys Tyr Ile Met Ala Cys Met
                        615
                                            620
Ser Ala Asp Leu Glu Val Val Thr Ser Thr Trp Val Leu Val Gly Gly
                    630
                                        635
Val Leu Ala Ala Leu Ala Ala Tyr Cys Leu Thr Thr Gly Ser Val Val
               645
                                    650
Ile Val Gly Arg Ile Ile Leu Ser Gly Arg Pro Ala Ile Val Pro Asp
                                665
Arg Glu Phe Leu Tyr Gln Glu Phe Asp Glu Met Glu Glu Cys Ala Ser
                            680
His Leu Pro Tyr Ile Glu Gln Gly Met Gln Leu Ala Glu Gln Phe Lys
                        695
Gln Lys Ala Leu Gly Leu Leu Gln Thr Ala Thr Lys Gln Ala Glu Ala
                   710
                                        715
Ala Ala Pro Val Val Glu Ser Lys Trp Arg Ala Leu Glu Thr Phe Trp
                                   730
Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu Ala Gly
           740
                                745
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Leu Ser Thr Leu Pro Gly Asn Pro Ala Ile Ala Ser Leu Met Ala Phe
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Thr Ala Ser Ile Thr Ser Pro Leu Thr Thr Gln Ser Thr Leu Leu Phe
                       775
Asn Ile Leu Gly Gly Trp Val Ala Ala Gln Leu Ala Pro Pro Ser Ala
                   790
                                      795
Ala Ser Ala Phe Val Gly Ala Gly Ile Ala Gly Ala Ala Val Gly Ser
               805
                                  810
                                                      815
Ile Gly Leu Gly Lys Val Leu Val Asp Ile Leu Ala Gly Tyr Gly Ala
           820
                              825
                                                  830
Gly Val Ala Gly Ala Leu Val Ala Phe Lys Val Met Ser Gly Glu Met
       835
                          840
                                              845
Pro Ser Thr Glu Asp Leu Val Asn Leu Leu Pro Ala Ile Leu Ser Pro
                       855
                                          860
Gly Ala Leu Val Val Gly Val Val Cys Ala Ala Ile Leu Arg Arg His
865
                   870
                                      875
Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu Ile Ala
               885
                                  890
Phe Ala Ser Arg Gly Asn His Xaa Ser Pro Thr His Tyr Val Pro Glu
           900
                              905
Ser Asp Ala Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu Thr Ile
                           920
Thr Gln Leu Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp Cys Ser
                       935
Thr Pro Cys Ser Gly Ser Trp Leu Arg Asp Val Trp Asp Trp Ile Cys
                   950
                                      955
Thr Val Leu Thr Asp Phe Lys Thr Trp Leu Gln Ser Lys Leu Leu Pro
               965
                                  970
Gln Leu Pro Gly Val Pro Phe Phe Ser Cys Gln Arg Gly Tyr Lys Gly
           980
                              985
                                                  990
Val Trp Arg Gly Asp Gly Ile Met Gln Thr Thr Cys Pro Cys Gly Ala
       995
                                             1005
                          1000
Gln Ile Thr Gly His Val Lys Asn Gly Ser Met Arg Ile Val Gly Pro
                      1015
                                         1020
Lys Thr Cys Ser Asn Thr Trp His Gly Thr Phe Pro Ile Asn Ala Tyr
                  1030
                                     1035
Thr Thr Gly Pro Cys Thr Pro Ser Pro Ala Pro Asn Tyr Ser Arg Ala
              1045
                                 1050
Leu Trp Arg Val Ala Ala Glu Glu Tyr Val Glu Val Thr Arg Val Gly
           1060
                              1065
Asp Phe His Tyr Val Thr Gly Met Thr Thr Asp Asn Val Lys Cys Pro
       1075
                         1080
                                             1085
Cys Gln Val Pro Ala Pro Glu Phe Phe Thr Glu Val Asp Gly Val Arg
                      1095
                                         1100
Leu His Arg Tyr Ala Pro Ala Cys Arg Pro Leu Leu Arg Glu Glu Val
                  1110
                                      1115
Thr Phe Gln Val Gly Leu Asn Gln Tyr Leu Val Gly Ser Gln Leu Pro.
              1125
                                  1130
Cys Glu Pro Glu Pro Asp Val Ala Val Leu Thr Ser Met Leu Thr Asp
                              1145
Pro Ser His Ile Thr Ala Glu Thr Ala Lys Arg Arg Leu Ala Arg Gly
                         1160
                                             1165
Ser Pro Pro Ser Leu Ala Ser Ser Ser Ala Ile Gln Leu Ser Ala Pro
                       1175
                                          1180
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Ser Leu Lys Ala Thr Cys Thr Thr His His Val Ser Pro Asp Ala Asp
                    1190
Leu Ile Glu Ala Asn Leu Leu Trp Arg Gln Glu Met Gly Gly Xaa Ile
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                                    1210
Thr Arg Val Glu Ser Glu Asn Lys Val Val Leu Asp Ser Phe Asp
                                1225
Pro Leu Arg Ala Glu Glu Asp Glu Arg Glu Val Ser Val Pro Ala Glu
                            1240
                                                1245
Ile Leu Arg Lys Ser Lys Lys Phe Pro Ala Ala Met Pro Ile Trp Ala
                        1255
                                            1260
Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp
                    1270
                                        1275
                                                             1280
Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala
                1285
                                    1290
                                                        1295
Pro Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu
            1300
                                1305
                                                     1310
Ser Ser Val Ser Ser Ala Leu Ala Glu Leu Ala Thr Lys Thr Phe Gly
                            1320
                                                1325
Ser Ser Glu Ser Ser Ala Val Asp Ser Gly Thr Ala Thr Ala Leu Pro
                        1335
                                            1340
Asp Gln Ala Ser Asp Asp Gly Asp Lys Gly Ser Asp Val Glu Ser Tyr
                    1350
                                        1355
Ser Ser Met Pro Pro Leu Glu Gly Glu Pro Gly Asp Pro Asp Leu Ser
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Asp Gly Ser Trp Ser Thr Val Ser Glu Glu Ala Ser Glu Asp Val Val
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Cys Cys
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<211> 4182
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<221> variation
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<223> n = T or C
<221> variation
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<223> n = A or G
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Gln Asp Ile Gln Pro Ala Ile Gln Ser Ser Trp Pro Lys Leu Glu Gln
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Phe Trp Ala Lys His Met Trp Asn Phe Ile Ser Gly Ile Gln Tyr Leu
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Leu Leu Asn Ile Met Gly Gly Trp Leu Ala Ser Gln Ile Ala Pro Pro
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Ala Gly Ala Thr Gly Phe Val Val Ser Gly Leu Val Gly Ala Ala Val
Gly Ser Ile Gly Leu Gly Lys Ile Leu Val Asp Val Leu Ala Gly Tyr
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Gly Ala Gly Ile Ser Gly Ala Leu Val Ala Phe Lys Ile Met Ser Gly
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                                        155
Glu Lys Pro Thr Val Glu Asp Val Asn Leu Leu Pro Ala Ile Leu
                165
                                    170
Ser Pro Gly Ala Leu Val Val Gly Val Ile Cys Ala Ala Ile Leu Arg
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Arg His Val Gly Pro Gly Glu Gly Ala Val Gln Trp Met Asn Arg Leu
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                            200
                                                205
Ile Ala Phe Ala Ser Arg Gly Asn His Ala Ser Pro Thr His Tyr Val
                       215
                                           220
Pro Glu Ser Asp Ala Ala Arg Val Thr Gln Ile Leu Ser Ser Leu
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                                       235
Thr Ile Thr Gln Leu Lys Arg Leu His Gln Trp Ile Asn Glu Asp
               245
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Cys Ser Thr Pro Cys
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